REMARKS/ARGUMENTS

Claims 14, 25 and 38 have been amended. Subsequent to the entry of the present amendment, claims 2-33 and 38 are pending and at issue. These amendments and additions add no new matter as the claim language is fully supported by the specification and original claims.

I. Rejections under 35 U.S.C. §112, Second Paragraph

A. Claims 2-33 and 38 are rejected under 35 U.S.C. §112, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse this rejection.

With regard to claims 14 and 15, the Office Action alleges the phrase s "a plurality of he discrete locations" and "a plurality of discrete protein locations" are vague because it is unclear whether the claims are referring to the plurality of discrete protein locations of claim 38 or whether a separate plurality of discrete locations exist.

Applicants have amended claim 14 to remove the phrase "comprised of a plurality of he discrete locations". Accordingly, Applicant requests withdrawal of the rejection of claims 14 and 15.

With regard to claim 38, the Office Action alleges that the claim is vague because it is unclear whether the "a discrete protein enriched location" recited in line 2 of part e) of the claim is the same discrete protein enriched location created by depositing each fraction at a discrete location in part b. The Office Action further alleges that there is insufficient antecedent basis for the claim limitations "the chemical composition" in line 3 of part e, and "the corresponding" in line 4 of part e.

Applicants have amended claim 38 to state "a chemical composition" and replaced the term "corresponding" with "selected", which should now make claim 38 clear. Accordingly, Applicant requests withdrawal of this rejection.

With regard to claim 25, the Office Action alleges it is unclear whether the method of claim 38 further comprises maintaining the separated proteins in a separated state or whether the step of depositing includes the step of maintaining.

Applicants have amended claim 25 to clarify that the step of depositing includes the step of maintaining. Accordingly, Applicant requests withdrawal of this rejection.

II. Rejections under 35 U.S.C. §103

A. Claims 2-5, 10, 14-17, 20-26, 29-33 and 38 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,579,721) in view of Carron (US 5,693,152). This rejection is respectfully traversed.

The Office action alleges that "Natan et al. teaches a method for analyzing the protein content of a biological sample (col. 10, lines 40-47 describe a sandwich assay, col. 10, line 52 describes the target analyte being a protein), comprising: separating proteins in a sample (separates target analyte based on chemical interaction, col. 23, lines 45-48; ligands for different target analyte must be separated in order for attachment at specific locations, col. 3, lines 23-26; ligands can be proteins, col. 10, lines 40-47); depositing proteins in a separate state at discrete locations on a solid substrate (ligands are attached at specific locations, therefore ligands can be samples in each well which are maintained without cross contamination, col. 25, lines 1-4); contacting the separated proteins deposited at the plurality of discrete protein enriched locations with probes under conditions suitable to form a capture probe/protein complex at one or more discrete locations (col. 3, lines 47-54; col. 10, lines 58-64; at col. 13, lines 45-52 any one of the

participants can be immobilized to the substrate surface, a ligand is then bound to the immobilized receptor, protein); contacting the complexes with a Raman-active probe construct that binds to the complex (col. 3, lines 54-63; col. 13, lines 45-52, and Au-conjugated antibody is conjugated with the ligand, which is bound to the immobilized receptor, protein); and detecting Raman spectra produced by the probe construct/protein complexes at the plurality of discrete locations, wherein a Raman spectrum from at a discrete location provides information about the chemical composition of a protein the corresponding discrete protein enriched location by analyzing the protein content of a complex biological sample (col. 23, lines 58-61 discloses SERS detection; Fig. 12 discloses an amplified detection after an unamplified detection; furthermore a change in resonance is detected as the target is brought in contact with the Raman-active probe, therefore the SERS detection occurs before and after contacting the proteins with captured probes and Raman active probes, col. 18, lines 1-5). Natan et al. fail to teach chromatographically separating proteins and protein fragments in the sample into a plurality of fractions."

The Office Action further alleges that "Carron teaches chromatographically separating compounds in a sample into a plurality of fractions, each fraction containing an individual compound (col. 3, line 54- col. 4, line 1), in order to perform chemical analysis of raw samples and separate the component to be analyzed." The Office Action finally alleges that "it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the separation of proteins of Natan et al., chromatographic separating compounds into a plurality of fractions, each fraction containing an individual compound as taught by Carron, in order to allow the different ligands (proteins) to more accurately separated analyzed chemical interactions of different proteins."

To establish a *prima facie* case of obviousness, the following three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference(s) as proposed by

the Examiner; (2) there must be a reasonable expectation of success and (3) the prior art reference(s) must teach or suggest all of the claim limitations.

First, Applicants submit that the prior art references fail to teach or suggest all of the claim limitations. The teachings of Natan appear to be limited to physical separation of a sample into smaller portions or allotments, such as by distributing or allotting portions of a sample into individual microwells that are not fluidically connected. Natan contemplates dividing a sample into smaller volume allotments, which are each distributed into an array of microwells for the purpose of conducting separate chemical reactions in the individual microwells. While the samples of Natan are divided into allotments of smaller volume and distributed into individual microwells, the proteins in the sample are not in any way distinguished from each other prior to separation. The Office Action correctly points out that Natan et al. fail to teach chromatographically separating proteins and protein fragments in the sample into a plurality of fractions. The addition of Carron does not cure this defect. Applicants respectfully disagree with the Office Action allegation that "Carron teaches chromatographically separating compounds in a sample into a plurality of fractions, each fraction containing an individual compound". A closer review of Carron shows that it discloses "a generalized molecule-specific means of detection that can be applied to all existing separation systems" and that it's "invention consists of the modification of SERS substrates by the application of a stabilized coating that also reproduces or mimics the separation specific process being utilized." (Carron, Abstract). The Carron device is a SERS separation cell 3 having an input channel 1 for inflow from an external separation device. A transparent SERS substrate 5 is used with Raman excitation provided by an external laser source that is coupled to the transparent coated SERS substrate 5 (Carron, col. 4, lines 14-24, Figure 1) (emphasis added). Carron states that the device "has been employed in the detection of a separation from a gas chromatograph (Carron, col. 4, lines 63-64). As can be seen from this discussion, the Carron device uses gas that has been separated prior to introduction into the device for analysis. Nowhere is it disclosed that Carron teaches

"chromatographically separating compounds in a sample into a plurality of fractions" nor does it teach that "each fraction containing an individual compound". Accordingly, it is submitted that the cited references, either separately or in combination, fail to teach or suggest all of the claim limitations.

Second, Applicants submit that there is no reasonable expectation of success to combine the references to achieve the claimed invention. Natan et al. discloses depositing a protein in microwell arrays, but not separating compounds in a sample into a plurality of fractions with each fraction containing an individual compound. As discussed above, Carron also does not disclose this. Accordingly, there is no reasonable expectation of success that the combination of the references could not achieve the claimed invention.

For at least for the reasons set forth above, it is submitted that the cited references, either separately or in combination, fail to teach or suggest all of the claim limitations. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

B. Claims 6-9 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,579,721) in view of Carron (US 5,693,152), as applied to claim 38, further in view of Grow (US 6,040,191). This rejection is respectfully traversed.

As discussed above, Applicants have shown that Natan et al. and Carron fail to teach each and every element of claim 38, and there is there is no motivation to combine their teachings. Claims 6-9 ultimately depend upon claim 38. Claims 6-9 should be allowable for at least those same reasons discussed above. The addition of Grow does not provide the teachings that are missing from Natan et al. and Carron to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 6-9. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

C. Claims 11-13 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,579,721) in view of Carron (US 5,693,152), as applied to claim 38, further in view of Avseenko et al. (Immobilization of Proteins in Immunochemical Microarrays Fabricated by Electrospray Deposition, Analytical Chemistry, 2001, 73, 6047-6052). This rejection is respectfully traversed.

As discussed above, Applicants have shown that Natan et al. and Carron fail to teach each and every element of claim 38, and there is there is no motivation to combine their teachings. Claims 11-13 ultimately depend upon claim 38. Claims 11-13 should be allowable for at least those same reasons discussed above. The addition of Avseenko et al. does not provide the teachings that are missing from Natan et al. and Carron to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 11-13. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

D. Claims 18 and 19 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,579,721) in view of Carron (US 5,693,152), as applied to claim 38, further in view of Storhoff et al. (US 2004/0053222). This rejection is respectfully traversed.

As discussed above, Applicants have shown that Natan et al. and Carron fail to teach each and every element of claim 38, and there is there is no motivation to combine their teachings. Claims 18 and 19 ultimately depend upon claim 38 (through claim 17). Claims 18 and 19 should be allowable for at least those same reasons discussed above. The addition of Storhoff et al. does not provide the teachings that are missing from Natan et al. and Carron to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 18 and 19. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

E. Claims 27 and 28 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,579,721) in view of Carron (US 5,693,152), as applied to claim 38, further in view of Nelson et al. (US 5,955,729). This rejection is respectfully traversed.

As discussed above, Applicants have shown that Natan et al. and Carron fail to teach each and every element of claim 38, and there is there is no motivation to combine their teachings. Claims 27 and 28 ultimately depend upon claim 38. Claims 27 and 28 should be allowable for at least those same reasons discussed above. The addition of Storhoff et al. does not provide the teachings that are missing from Natan et al. and Carron to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 27 and 28. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

III. Conclusion

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved. No fee is believed due in connection with this Response. However, The Commissioner is hereby authorized to charge any fees that may be associated with this communication, or credit any overpayment to Deposit Account No. 07-1896.

Respectfully submitted,

Date: October 17, 2005

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER RUDNICK GRAY CARY US LLP
ATTORNEYS FOR INTEL CORPORATION
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer No. 28213